

APPLICANT(S): GEWIRTZ, Alan M.

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## **REMARKS**

The present response is intended to be fully responsive to all points of rejection raised by the Examiner and is believed to place the application in condition for allowance. Favorable reconsideration and allowance of the application is respectfully requested.

### **Status of Claims**

Claims 1-9, 11-13, 15-19, 21-24, 26-30, 32-35, 37-42, 44-48, and 50-60 are pending in the application. Claims 50-60 were withdrawn. Claims 1-9, 11-13, 15-19, 21-24, 26-30, 32-35, 37-42, 44-48 have been rejected. Claims 1, 4, 6, 11, 15, 21, 26, 32, 37, and 44 are amended herein. Support for amendments can be found throughout the specification as filed and specifically in paragraph 61 of the published application. Claims 61-68 have been added. Support for claims 61-68 can be found throughout the specification as filed and specifically in claim 1 as filed. Applicants assert that no new matter has been introduced.

## **CLAIM REJECTIONS**

### **35 U.S.C. § 102 Rejections**

In the Office Action, the Examiner rejected claims 1, 6, 9, and 15 under 35 U.S.C. § 102(b), as allegedly being anticipated by Taylor *et al.* (U.S. Patent 6,140,125) (“Taylor”). Specifically, the Examiner asserts that Taylor disclosed “inhibition of Bcl-6 in cells via administration of antisense compounds targeting Bcl-6.”

Applicants have amended the claims, and the amended claims are directed to a nucleic acid molecule corresponding to SEQ ID NO: 6. Nowhere does Taylor disclose or teach this sequence. Specifically, Taylor does not target nucleotides 1190-1222 of Bcl-6 (SEQ ID NO: 6), which is the target of the present invention.

Rather, Taylor targets various other portions of the bcl-6 gene with phosphorothioate oligonucleotides having 2'-MOE wings and a deoxy gap and show varying levels of bcl-6 mRNA inhibition. In fact, Taylor’s antisense molecule directed to the closest targets (1151

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and 1231, SEQ ID NO: 44 and 45 of Taylor, respectively) show very low suppression of bcl-6 mRNA levels (2 and 0%, respectively, Taylor Table 1).

Since Taylor disclose or teach SEQ ID NO: 6, Taylor does not anticipate the claimed invention.

The Examiner alleged that a portion of SEQ ID NO: 6 may reasonably be interpreted as comprising a single nucleotide. Applicants note that Applicants have amended the claims and the amended claims recite “a molecule complementary to the sequence set forth in SEQ ID NO: 6,” which does not refer to a single nucleotide. Furthermore, the Examiner acknowledged in the Office Action dated August 4, 2009 that “SEQ ID NO: 6 is free of the prior art.” *See* page 2, line 12 of the Office Action. Therefore, Applicant respectfully requests withdrawal of the rejection.

### **35 U.S.C. § 103 Rejections**

In the Office Action, the Examiner rejected claims 1-49 under 35 U.S.C. § 103(a), as being obvious over Taylor and Opalinska *et al.* (*Blood*, vol. 102 (11):137A-138A, 2003) (“Opalinska”) in view of Tuschl *et al.* (U.S. 2004/0259247) (“Tuschl”), Noonberg *et al.* (U.S. 5,624,803), and Li *et al.* (U.S. 2002/0114784) (“Li”). Applicant respectfully disagrees for the reasons set forth below.

None of the references describe any use of the specific sequence SEQ ID NO: 6 nor of a 21-23 nucleotide-long fragment of SEQ ID NO: 6, and not in a method of inducing apoptosis or in a method of treating a subject with lymphoma. Therefore, the combination of references does not comprise all of the claim limitations.

In addition, the Opalinska reference describes the Applicant’s own work (see attached Declaration) and was submitted to the Annual Meeting of Hematology less than one year before the priority date of the subject application. The Opalinska reference therefore is not a prior-art. Applicant therefore respectfully requests that the rejection be withdrawn.

Further, Taylor does not provide any motivation for a skilled artisan to use SEQ ID NO: 6 (complementary to 1190-1222 of bcl-6) as antisense to bcl-6, because they do not provide data for or even specifically mention that particular sequence within bcl-6. Taylor even teaches away from using an antisense corresponding to SEQ ID NO: 6 to inhibit bcl-6,

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because Taylor showed that applying antisense to that region of bcl-6 was not effective in inhibiting bcl-6 mRNA (see Taylor, column 43, Table 1, Target Sites 1151 and 1231 showing only 2 and 0% inhibition, respectively). In addition, the data presented herein are unexpected in view of Taylor in combination with the other references in that SEQ ID NO: 6 decreased bcl-6 mRNA 7-fold (i.e. 700%, see Fig. 6), decreased bcl-6 protein levels by 80% (Fig. 7), and resulted in a 50% drop in cell viability within 24 hours. This contrasts with the data presented by Taylor, showing a *maximum* mRNA inhibition of 62% in a different portion of the gene. Taylor does not have data for antisense targeting the portion of bcl-6 complementary to SEQ ID NO: 6, showed no mRNA inhibition in the neighboring region and did not present data demonstrating the effects of their antisense sequences on bcl-6 protein levels or on cell viability. Since none of the other references remedy the deficiencies of Taylor by suggesting SEQ ID NO: 6 as useful in downregulating bcl-6, Applicant asserts that the claims are not obvious in view of the cited references.

Applicant therefore respectfully requests withdrawal of the rejection.

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### **CONCLUSION**

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 50-3355.

Respectfully submitted,

/Mark S. Cohen/

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Dated: June 28, 2010

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